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(FILE 'HOME' ENTERED AT 10:17:24 ON 27 APR 2005)

FILE 'REGISTRY' ENTERED AT 10:17:34 ON 27 APR 2005

E BISPHOSPHONATE

L1 116 S E3-E4

FILE 'CAPLUS' ENTERED AT 10:18:36 ON 27 APR 2005

L2 8738 S L1 OR ALENDRONATE OR RISEDRONATE OR TILUDRONATE OR PAMIDRONAT
E ZWITTERIONIC PHOSPHOLIPID

FILE 'REGISTRY' ENTERED AT 10:20:18 ON 27 APR 2005

E ZWITTERIONIC PHOSPHOLIPID

E PHOSPHOLIPID

FILE 'CAPLUS' ENTERED AT 10:20:46 ON 27 APR 2005

L3 114023 S E3

=> s l2(l)l3

L4 9 L2(L)L3

=> d ibib 1-3

L6 ANSWER 1 OF 3 USPATFULL on STN

ACCESSION NUMBER: 2003:251608 USPATFULL

TITLE: Unique compositions of zwitterionic phospholipids and bisphosphonates and use of the compositions as bisphosphate delivery systems with reduced GI toxicity

INVENTOR(S): Lichtenberger, Lenard M., Houston, TX, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003176397	A1	20030918
APPLICATION INFO.:	US 2003-366155	A1	20030213 (10)
RELATED APPLN. INFO.:	Division of Ser. No. US 2001-827493, filed on 6 Apr. 2001, PENDING		

divisional of

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-195562P	20000407 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	ROBERT W. STROZIER, SUITE 930, 2925 BRIARPARK DRIVE, HOUSTON, TX, 77042	
NUMBER OF CLAIMS:	45	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	9 Drawing Page(s)	
LINE COUNT:	1366	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 2 OF 3 USPATFULL on STN

ACCESSION NUMBER: 2002:273743 USPATFULL

TITLE: Devices and methods for management of bone density

INVENTOR(S): Chan, Tai-Wah, Palo Alto, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002151876	A1	20021017
APPLICATION INFO.:	US 2002-71821	A1	20020207 (10)

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	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-267323P	20010207 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	DURECT CORPORATION, 10240 BUBB ROAD, CUPERTINO, CA, 95014	
NUMBER OF CLAIMS:	14	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	2 Drawing Page(s)	
LINE COUNT:	1579	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 3 OF 3 USPATFULL on STN

ACCESSION NUMBER: 2002:37883 USPATFULL

TITLE: Unique compositions of zwitterionic phospholipids and bisphosphonates and use of the compositions as bisphosphate delivery systems with reduced GI toxicity

INVENTOR(S): Lichtenberger, Lenard M., Houston, TX, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002022603	A1	20020221
APPLICATION INFO.:	US 2001-827493	A1	20010406 (9)

instant application

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-195562P	20000407 (60)
DOCUMENT TYPE:	Utility	

FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: ROBERT W STROZIER, PLLC, 2925 BRIARPARK, SUITE 930,
HOUSTON, TX, 77042
NUMBER OF CLAIMS: 45
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 9 Drawing Page(s)
LINE COUNT: 1368
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> s 12(1)13

L4 9 L2(L)L3

=> d ibib abs 1-9

L4 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:449457 CAPLUS
DOCUMENT NUMBER: 137:24122
TITLE: Hair formulations containing phospholipids and proteins
INVENTOR(S): Poppe, Elisabeth; Weser, Gabriele
PATENT ASSIGNEE(S): Hans Schwarzkopf GmbH & Co. Kg, Germany
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002045664	A1	20020613	WO 2001-EP13922	20011128
W: AU, JP, US				
RW: AT, BE, CH, PT, SE, TR				
DE 10060814	A1	20020613	DE 2000-10060814	20001207
AU 2002017064	A5	20020618	AU 2002-17064	20011128
PRIORITY APPLN. INFO.:			DE 2000-10060814	A 20001207
			WO 2001-EP13922	W 20011128

OTHER SOURCE(S): MARPAT 137:24122

AB The invention relates to a novel use of phospholipids which significantly improves the restructuring of fibers, especially keratin fibers, and the fastness of keratin fibers. Thus, a hair spray contained Eumulgin B2 0.3, cetylstearyl alc. 3.3, iso-Pr myristate 0.5, Lamesoft PO65 0.5, Dehyquart A-CA 2.0, Salcare SC-96 1.0, citric acid 0.4, Gluadin WQ 2.0, pyridoxine 1.0, linoleamideopropyl PG-dimonium chloride phosphate 0.7, Phenonip 0.8, and water to 100%.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:762801 CAPLUS
DOCUMENT NUMBER: 135:308912
TITLE: Unique compositions of zwitterionic phospholipids and bisphosphonates and use of the compositions as bisphosphate delivery systems with reduced GI toxicity
INVENTOR(S): Lichtenberger, Lenard M.
PATENT ASSIGNEE(S): Board of Regents of the University of Texas System, USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001076577	A2	20011018	WO 2001-US11375	20010406
WO 2001076577	A3	20020613		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,				

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BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2405360	AA	20011018	CA 2001-2405360	20010406
US 2002022603	A1	20020221	US 2001-827493	20010406
EP 1267890	A2	20030102	EP 2001-924814	20010406

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2004517800	T2	20040617	JP 2001-574095	20010406
BR 2001010316	A	20050118	BR 2001-10316	20010406
US 2003176397	A1	20030918	US 2003-366155	20030213

PRIORITY APPLN. INFO.: US 2000-195562P P 20000407
US 2001-827493 A3 20010406
WO 2001-US11375 W 20010406

OTHER SOURCE(S): MARPAT 135:308912

AB Compns. and methods for treating osteoporosis using the compns. are disclosed where the compns. have reduced gastrointestinal (GI) toxicity and improved bioavailability and include a bisphosphonate and zwitterionic **phospholipid**. The compns. further comprise a colloidal metal, a metal complex, or a mixture or combination thereof. For example, 20 mg of dipalmitoylphosphatidylcholine (DPPC) and a pure PC (Phospholipon 90 G) were dissolved in chloroform in sep. tubes, and dried. A solution of 60 mg/mL of **pamidronate** in saline adjusted to pH 7 was prepared and added to each of the tubes, one containing the DPPC film and the other containing the PC film. The PC-**pamidronate** mixture was then sonicated for 5 min at room temperature, while the DPPC-**pamidronate** mixture was sonicated for 5 min at > 42° for C, about 45. The results of the example are shown in Figure 7 and described previously.

L4 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:789614 CAPLUS

DOCUMENT NUMBER: 134:290229

TITLE: Effect of bisphosphonates on surface hydrophobicity and phosphatidylcholine concentration of rodent gastric mucosa

AUTHOR(S): Lichtenberger, Lenard M.; Romero, Jimmy J.; Gibson, George W.; Blank, Marion A.

CORPORATE SOURCE: Department of Integrative Biology & Pharmacology, The University of Texas Medical School at Houston, Houston, TX, 77030, USA

SOURCE: Digestive Diseases and Sciences (2000), 45(9), 1792-1801

CODEN: DDSCDJ; ISSN: 0163-2116

PUBLISHER: Kluwer Academic/Plenum Publishers

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Bisphosphonates are a family of chemical related zwitterionic mols. that are used clin. to retard bone resorption in individuals with osteoporosis and associated skeletal diseases. Inflammation and ulceration of the upper gastrointestinal tract by a mechanism that relates to a topical irritant action is associated with the consumption of some bisphosphonates. In the present study, the authors investigated the effects of 3 bisphosphonate mols., **pamidronate**, **alendronate**, and **risedronate** on the surface hydrophobicity and phosphatidylcholine (PC) concentration of the antral mucosa. The authors also examined how these surface changes related to mucosal injury in an established rat model, in which the test compds. were administered in combination with indomethacin. The authors initially determined that a combination of **pamidronate** (300 mg/kg) and indomethacin (40 mg/kg) induced a reduction in mucosal surface hydrophobicity and macroscopic lesion formation by 15 min and mucosal PC concentration by 30 min, with the magnitude of these changes increasing over the 4-h study period. An equivalent dose of **alendronate** or **risedronate** in combination with indomethacin produced modest or no macroscopic injury, resp., to the antral mucosa over the 4-h study, although the bisphosphonates clearly induced surface injury and some glandular necrosis when examined at the light microscopic level. These bisphosphonates also induced modest decreases in antral surface hydrophobicity and mucosal PC concentration that appeared to be related to their injurious potential. In conclusion, the variable toxicity of bisphosphonates to the antral mucosa appears to be associated with their

September, 2000

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ability to compromise the surface hydrophobic phospholipid

barrier of the tissue, with pamidronate > > >

alendronate > risedronate. This bisphosphonate effect

on the surface barrier may trigger the development of mucosal injury and possible ulceration.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:745745 CAPLUS

DOCUMENT NUMBER: 132:59008

TITLE: Inhibition of β 2glycoprotein I binding to anionic phospholipids: A strategy for the development of antiphospholipid syndrome-specific drugs

AUTHOR(S): Kohles, Joseph D.; Petersheim, Matthew; Debari, Vincent A.

CORPORATE SOURCE: The Rheumatology Laboratory, Department of Medicine, St. Joseph's Hospital and Medical Center, Paterson, NJ, 07503, USA

SOURCE: Drug Design and Discovery (1999), 16(3), 227-236
CODEN: DDDIEV; ISSN: 1055-9612

PUBLISHER: Harwood Academic Publishers

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The binding of β 2glycoprotein I (β 2GPI) to anionic phospholipids (PL) leads to the presentation of one or more epitopes recognized by autoantibodies from patients with antiphospholipid syndrome (APS). The inhibition of β 2GPI binding to PL mixts. coated on polystyrene microtiter wells (MTW) and to large, multilamellar PL vesicles (LMV) was examined. Inhibitors included phosphorylated monosaccharide metabolites, myo-inositol monophosphate (IMP), hexaphosphate (IHP) and hexasulfate (IHS), pyrophosphate (PPi), Me bisphosphonate (MBP) and Ph phosphonate, and a series of carboxylic and aromatic sulfonic acids. Inhibitors were incubated with β 2GPI at 37° for 2 h either with dimyristoylphosphatidic acid, 80%/dimyristoylphosphatidyl choline, 20% (DMPA/DMPC) coated on MTW or in a suspension of LMV. Phospholipid-bound β 2GPI to PA/PC on MTW was detected using an immunoassay based on rabbit anti- β 2GPI; free β 2GPI (not bound to LMV) was detected by fluorescence spectroscopy. Inhibition was studied over the range 0.01-9.0 μ moles/10-4L (0.1-90 mM). Inhibition at maximum concentration in the MTW system ranged from 0.1% (for ADP) to > 94% (for IHP). IHP also provided the greatest inhibition in the LMV system (76%) and was also effective in displacing β 2GPI already bound to PL surfaces (.apprx.50% displaced at 0.25 mM). These data suggest that a strategy for development of therapeutic agents for APS may be based on the use of small cyclic, organic oligoanions such as inositol derivs. to act as ligands for lysine residues at the PL binding site of β 2GPI.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1995:706030 CAPLUS

DOCUMENT NUMBER: 123:102748

TITLE: The antiosteoporotic activity of amine-carboxyboranes in rodents

AUTHOR(S): Rajendran, K G.; Chen, S Y.; Sood, A.; Spielvogel, B F.; Hall, I H.

CORPORATE SOURCE: School Pharmacy, University North Carolina, Chapel Hill, NC, 27599-7360, USA

SOURCE: Biomedicine & Pharmacotherapy (1995), 49(3), 131-40
CODEN: BIPHEX; ISSN: 0753-3322

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In vitro studies using CF1 mouse pup calvaria and rat UMR-106 osteosarcoma cells showed that amine-carboxyborane derivs. reduced the loss of intracellular calcium into the growth medium. Amine-carboxyborane derivs. were more effective than calcitonin or simple boron salts. Calcium

incorporation into these cells and proline incorporation into collagen were accelerated in the presence of the amine-carboxyboranes. The amine-carboxyborane derivs. effectively inhibited lysosomal and proteolytic enzymes as well as activities of serine elastase, prostaglandin cyclooxygenase, and 5'-lipoxygenase in mouse macrophages, human polymorphonuclear leukocytes, and Be Sal cells. IC50 values were in the range 10-6M. In lactating ovariectomized female rats after administration of amine-carboxyboranes for 14 days at 8 mg/kg/day orally, the femur and humerus showed increased volume, weight, d. and ash weight Serum calcium levels were elevated with min. redns. of serum inorg. phosphate levels. Femur calcium levels were elevated after treatment with the amine-carboxyborane derivs., but not with **etidronate**. Humerus total lipids after 14 days were slightly elevated, probably due to increased levels of triglycerides and **phospholipids**.

L4 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1992:549638 CAPLUS

DOCUMENT NUMBER: 117:149638

TITLE: Complex systems formation between iron, calcium, and magnesium and citric, succinic, and hydroxyethylidenediphosphonic acids.

AUTHOR(S): Butina, E. A.; Kapustyanskaya, Zh. V.; Pogrebnaya, V. L.; Tarasenko, A. G.; Tsymbal, E. P.; Gritsenko, I. K.; Kitaigorodskii, I. A.

CORPORATE SOURCE: Krasnodar. Politekh. Inst., Krasnodar, Russia

SOURCE: Izvestiya Vysshikh Uchebnykh Zavedenii, Pishchevaya Tekhnologiya (1992), (2), 52-3
CODEN: IVUPA8; ISSN: 0579-3009

DOCUMENT TYPE: Journal

LANGUAGE: Russian

AB Complexing in the title systems was studied in order to obtain information about the stability of obtained complexes and their possible use for destruction of metal-phospholipid complexes and their removal from vegetable oils. The stability consts. for such complexes as [Fe3+-citric acid]+, [Ca2+-citric acid]+, [Mg2+-citric acid]+, [Fe3+-succinic acid]+, [Ca2+-succinic acid]+, [Mg2+-succinic acid]+, [Fe3+-hydroxyethylidenediphosphonic acid]+, [Ca2+-hydroxyethylidenediphosphonic acid]+, and [Mg2+-hydroxyethylidenediphosphonic acid]+ were obtained and data are presented. It is concluded that use of succinic acid, forming the most stable complexes with the tested ions, may be the most prospective for hydration of oils with high levels of nonhydratable phospholipids.

L4 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1992:549637 CAPLUS

DOCUMENT NUMBER: 117:149637

TITLE: Comparative estimation of protonation constants of citric, succinic, and hydroxyethylidenediphosphonic acids

AUTHOR(S): Pogrebnaya, V. L.; Kapustyanskaya, Zh. V.; Butina, E. A.; Shakhrai, T. A.; Kitaigorodskii, I. A.; Volkov, O. N.; Sokolovskaya, T. M.

CORPORATE SOURCE: Krasnodar. Politekh. Inst., Krasnodar, Russia

SOURCE: Izvestiya Vysshikh Uchebnykh Zavedenii, Pishchevaya Tekhnologiya (1992), (2), 51-2
CODEN: IVUPA8; ISSN: 0579-3009

DOCUMENT TYPE: Journal

LANGUAGE: Russian

AB Comparative estimation of protonation consts. of the title acids showed that succinic and hydroxyethylidenediphosphonic acids were better complexons than citric acid. The data obtained suggest that solns. of these acids may be used for the destruction of nonhydratable phospholipid-metal complexes and their removal during hydration of vegetable oils.

L4 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1991:3833 CAPLUS

DOCUMENT NUMBER: 114:3833

TITLE: Inclusion of bisphosphonates into lipids of animal

cells
AUTHOR(S): Fominskaya, G. N.; Volkov, G. L.; Komissarenko, S. V.
CORPORATE SOURCE: Inst. Biokhim., Kiev, USSR
SOURCE: Doklady Akademii Nauk Ukrainskoi SSR, Seriya B:
Geologicheskie, Khimicheskie i Biologicheskie Nauki
(1990), (6), 84-6
CODEN: DNNADO; ISSN: 0201-8454

DOCUMENT TYPE: Journal
LANGUAGE: Russian

AB [14C]Methylenebisphosphonic acid (MBPA). administered i.p to rats, was incorporated into the total lipid exts. of the liver, spleen, and thymus gland for up to 6 h. It was assumed that hydrolysis products of MBPA were not formed. After 6 h administration of [14C]MBPA, for each micromole phosphatidylcholine, phosphatidylethanolmaine, phosphatidylinositol + phosphatidylserine, and sphingomyelin there were incorporated 2.9, 3.6, 1.9, and 13.1 nmol MBPA, resp. By known chemical and enzymic methods to cleave phosphatidylcholine, label was found in lysophosphatidylcholine, phosphatidic acid, phosphocholine, glycerophosphorocholione, and α -glycerophosphate, but not in glycerol, choline, or diglyceride. Evidently, bisphosphonates become incorporated into cell lipids via formation of bisphosphonate-containing phospholipid analogs.

L4 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1979:201452 CAPLUS

DOCUMENT NUMBER: 90:201452

TITLE: Effect of diphosphonates on hydroxyapatite formation induced by calcium-phospholipid-phosphate complexes
AUTHOR(S): Boskey, A. L.; Goldberg, M. R.; Posner, A. S.
CORPORATE SOURCE: Hosp. Spec. Surg., Cornell Univ., New York, NY, USA
SOURCE: Calcified Tissue International (1979), 27(1), 83-8
CODEN: CTINDZ; ISSN: 0171-967X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The diphosphonates, disodium ethane-1-hydroxy-1,1-diphosphonate and disodium dichloromethylene diphosphonate prevent hydroxylapatite (HA) formation in metastable calcium phosphate solns., induced by Ca-phospholipid-phosphate complexes and by the acidic phospholipids, phosphatidylserine and phosphatidylinositol. The diphosphonates act not only as HA crystal poisons but also as surfactants which probably change the nature of the lipid micelle and the charge and conformational properties of the lipid mols. The surfactants, Na dodecyl sulfate and Non-Idet P-40, like the diphosphonates, prevent HA formation by the acidic phospholipids and complexed lipids, but do not act as HA surface poisons. The lipid surfactant, lysophosphatidylserine did not induce HA formation from solution. The relevance of the ability of the diphosphonates to act as lipid surfactants to the in vivo use of these agents is discussed.

